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# Abnormal microcirculation and temperature in skin above tender points in patients with fibromyalgia

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## Abstract

*Objective*. Skin temperature and skin blood flow were studied above different tender points in 20 patients with fibromyalgia (FM) and 20 healthy controls.

*Methods*. Blood flow was measured by laser Doppler flowmetry and skin temperature was measured with an infrared thermometer.

*Results*. In the skin above the five tender points examined in each subject, we found an increased concentration of erythrocytes, decreased erythrocyte velocity and a consequent decrease in the flux of erythrocytes. A decrease in temperature was recorded above four of the five tender points.

*Conclusion*. Vasoconstriction occurs in the skin above tender points in FM patients, supporting the hypothesis that FM is related to local hypoxia in the skin above tender points.

KEY WORDS: Fibromyalgia, Skin blood flow, Laser flowmetry, Temperature, Algometry.

Fibromyalgia (FM) is one of the most frequent rheumatological diseases and one of the most controversial diagnoses in the field of rheumatology [1]. FM has a prevalence of 1–3% and occurs predominantly in females, commonly between the ages of 40 and 50 yr [2, 3].

The aetiopathology of FM is still unknown. Several factors are thought to interact: muscle overload, bad posture of the spine [4], disturbed sleep [5], psychogenic factors [6], local hypoxia [7, 8] and reduced levels of high-energy phosphate [9].

In 1973, Fassbender *et al*. [7] published a morphological study of FM and hypothesized that local hypoxia causes degenerative changes in the muscle. In 1986, this hypothesis was supported by the findings of Bengtsson *et al*. [9]. They reported decreased levels of adenosine diphosphate and phosphoryl creatine together with increased levels of adenosine monophosphate and creatine. Furthermore, they described discrete histopathological and histochemical changes in muscle biopsies [10]. Lund *et al*. [8] reported abnormal oxygen pressure at the muscle surface above trigger points.

Here, we describe changes in skin blood flow as revealed by the examination of skin temperature and tenderness and local blood flow in the skin above defined tender points determined by the Doppler method.

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## Patients and methods

Twenty FM patients (18 female, two male) with a mean age of 46 ± 2.5 (S.E.M.) yr (range 23–67 yr) were included in this study. They had presented symptoms for an average of 4 ± 1.1 yr (range 1–30 yr). The gender-matched control group (mean age 46 ± 4.4 yr, range 23–66 yr) consisted of 20 persons with no symptoms of muscular disease. The diagnosis of FM was based on the modified criteria of Müller [1] and the ACR criteria [11]. The mean number of positive tender points in the FM group was 16.1 ± 0.6.

Five selected pairs of tender points in the FM patient group and corresponding tender point locations in the control group were explored. Where data are given in this paper for a tender point, they refer to the average of the bilateral pair of tender points. The tender points were localized with reference to anatomical structures, as defined in the criteria [1]. Other tender or control points were not considered in this study.

All subjects had abstained from physical therapy, physical examination, vasoactive drugs and local vasoactive substances for at least 24 h before the study. The examination was performed at room temperature (24°C).

The blood flow in the skin above the defined tender points [trapezius, erector trunci (additional tender point

by Müller [1]), greater trochanter, knees and lateral epicondyle] was measured with a laser blood-flow monitor (MBF 3D; Moor Instruments, Axminister, UK). Laser Doppler flowmetry provides simple, non-invasive, real-time measurement of local blood flow. It makes use of the Doppler shift of laser light; moving blood cells reflect the light, resulting in a frequency shift, the amount of shift depending on the speed of the cells. The power spectrum density of the beat notes is determined by the concentration of red blood cells [12]. The erythrocyte concentration, the relative mean erythrocyte speed and the mean of the resulting erythrocyte flux can then be displayed in arbitrary units (AU). The data were stored automatically for later analysis. The MBF 3D monitor used a solid-state laser diode as the laser light source, and the emitted frequency was between 780 and 810 nm. Two glass fibres were used to transmit the laser light to the tissue and to collect the reflected light for detection by the MBF 3D monitor [13]. The area examined was approximately 2 $mm^2$. The penetration depth of the laser was 1 mm [14].

Skin temperature above defined tender points was measured using an infra-red thermometer (Ther Monitor C-1600 M; Linear Laboratories, Fremont, California, USA). This thermometer was calibrated in increments of 0.1°C. The distance between the probe and the tender point was 1 cm. The temperature was displayed digitally.

At the end of the examination, the pressure tolerance of the different tender points was measured with a pain pressure algometer [15]. The top of the algometer was placed on the tender point and the pressure was increased until the patient confirmed pain [16, 17].

Statistics were scored using SPSS 7.2 for Windows. Differences between FM patients and controls were tested for significance by the Mann–Whitney *U*-test for unpaired samples. A $P$ value of $<0.05$ was considered significant.

## Results

Significant differences were found between FM patients and controls in laser Doppler flowmetry. The erythrocyte concentration was higher in the skin above all measured tender points in FM patients than in the healthy controls. A significant increase in concentration of 33% was found at the lateral epicondyle (121.8 AU for FM patients *vs* 91.2 AU for controls; $P = 0.0032$) and of 56% at the knees (92.8 *vs* 59.4 AU, $P = 0.0002$) (Table 1). Erythrocyte speed was lower in the skin above all tender points examined in FM subjects compared with controls; the difference was least at the lateral epicondyle (34%; 11.3 AU for FM patients *vs* 17.1 AU for controls; $P < 0.0001$) and greatest at the erector trunci (43%; 12.7 *vs* 22.2 AU; $P < 0.0001$) (Table 2). The calculated flux was lower in the skin above all tender points in FM patients than in controls. The difference in flux was least above the lateral epicondyle (17%; 22.0 AU for FM patients *vs* 26.4 AU for controls; $P = 0.0212$). The largest difference was found above the erector trunci tender point, where the flux was reduced by 39% (25.2 *vs* 41.7 AU; $P < 0.0001$) (Table 3).

Surface skin temperature at four of the tender points was lower in FM patients than in controls (Table 4). The decrease was least at the greater trochanter (0.5°C; 32.4 *vs* 32.9°C; $P = 0.0857$) and greatest at the lateral epicondyle (1.2°C; 32.2 *vs* 33.4°C; $P < 0.0001$). The skin temperature at the knees was 0.3°C higher in FM patients (31.7°C) than in controls (31.4°C) ($P = 0.4791$) (Table 4).

The algometry results showed significantly lower pain thresholds at all five tender points in the patient group than in the controls (Table 5).

## Discussion

The main symptoms in FM are muscle pain and tenderness, which are difficult to measure. Until now there have been no objective parameters to support the dia-

TABLE 1. Relative erythrocyte concentration (AU; mean ± S.E.M.) in the skin above tender points in FM patients and controls

| Tender point | Controls | FM | Significance |
|---|---|---|---|
| Trapezius | 129.6 ± 6.7 | 147.0 ± 14.2 | $P = 0.8625$ |
| Erector trunci | 126.4 ± 14.4 | 138.9 ± 13.5 | $P = 0.3287$ |
| Greater trochanter | 117.9 ± 8.8 | 126.8 ± 8.2 | $P = 0.2385$ |
| Lateral epicondyle | 91.2 ± 5.8 | 121.8 ± 9.4 | $P = 0.0032$ |
| Knees | 59.4 ± 2.8 | 92.8 ± 8.2 | $P = 0.0002$ |

TABLE 2. Relative erythrocyte speed (AU; mean ± S.E.M.) in the skin above tender points in FM patients and controls

| Tender point | Controls | FM | Significance |
|---|---|---|---|
| Trapezius | 25.0 ± 1.3 | 15.3 ± 1.2 | $P < 0.0001$ |
| Erector trunci | 22.2 ± 1.7 | 12.7 ± 1.0 | $P < 0.0001$ |
| Greater trochanter | 17.1 ± 1.4 | 11.0 ± 1.1 | $P = 0.0005$ |
| Lateral epicondyle | 17.1 ± 1.2 | 11.3 ± 0.9 | $P < 0.0001$ |
| Knees | 16.5 ± 0.8 | 9.8 ± 0.8 | $P < 0.0001$ |

TABLE 3. Relative erythrocyte flux (AU; mean ± S.E.M.) in the skin above tender points in FM patient and controls

| Tender point | Controls | FM | Significance |
|---|---|---|---|
| Trapezius | 58.9 ± 3.3 | 36.8 ± 2.7 | $P < 0.0001$ |
| Erector trunci | 41.7 ± 1.9 | 25.2 ± 1.8 | $P < 0.0001$ |
| Greater trochanter | 34.0 ± 2.9 | 21.2 ± 1.9 | $P < 0.0001$ |
| Lateral epicondyle | 26.4 ± 1.7 | 22.0 ± 1.4 | $P = 0.0212$ |
| Knees | 17.8 ± 0.7 | 14.4 ± 1.1 | $P = 0.0002$ |

TABLE 4. Skin temperature (°C; mean ± S.E.M.) above tender points in FM patients and controls

| Tender point | Controls | FM | Significance |
|---|---|---|---|
| Trapezius | 34.8 ± 0.1 | 33.8 ± 0.2 | $P < 0.0001$ |
| Erector trunci | 34.7 ± 0.1 | 34.1 ± 0.2 | $P = 0.0195$ |
| Greater trochanter | 32.9 ± 0.2 | 32.4 ± 0.2 | $P = 0.0857$ |
| Lateral epicondyle | 33.4 ± 0.1 | 32.2 ± 0.2 | $P < 0.0001$ |
| Knees | 31.4 ± 0.2 | 31.7 ± 0.2 | $P = 0.4791$ |

TABLE 5. Algometry (kP/1.47 $cm^2$; mean ± S.E.M.) at tender points in FM patients (FM) and controls

| Tender point | Controls | FM | Significance |
|---|---|---|---|
| Trapezius | 5.5 ± 0.4 | 2.1 ± 0.1 | $P < 0.0001$ |
| Erector trunci | 7.1 ± 0.3 | 1.9 ± 0.1 | $P < 0.0001$ |
| Greater trochanter | 7.1 ± 0.3 | 2.3 ± 0.1 | $P < 0.0001$ |
| Lateral epicondyle | 4.9 ± 0.3 | 1.7 ± 0.1 | $P < 0.0001$ |
| Knees | 7.0 ± 0.3 | 1.6 ± 0.1 | $P < 0.0001$ |

gnosis of FM. One reason is that the cause and pathogenesis of FM are as yet unknown.

Studies of the pathogenesis of FM have been concentrated mainly in six areas: (i) muscular and microcirculatory changes; (ii) changes in serotonin metabolism; (iii) neuroendocrinological changes; (iv) changes in function of the autonomic nervous system; (v) sleep disturbances; and (vi) psychological and psychiatric aberrations [18].

Our hypothesis is that FM originates in muscular and microcirculatory disturbances. The aim of this study was to provide evidence for changes in skin blood flow above defined tender points. Our study showed a higher erythrocyte concentration, decreased erythrocyte speed and decreased flux of erythrocytes in the skin and lower skin temperature above the tender points in FM patients than in healthy controls. The pain at the tender points in FM patients correlated with the measured reduction in local blood flow. We conclude that blood flow is disturbed, i.e. reduced, in the skin above the tender points we examined in the muscle of FM patients. This may result in an imbalance between oxygen supply and demand. Local hypoxia and a decrease in the concentration of high-energy phosphate occur, and morphological changes will result, as described by the following authors: Fassbender and Wegner [7] examined muscle biopsies from FM patients and reported step-wise destruction of myofilaments and swollen endothelial cells. These changes are probably associated with the relative hypoxia of the muscle cells in FM patients. It is not known whether the swollen endothelial cells are causative or symptomatic of hypoxia. Bengtsson *et al.* [10] found 'moth-eaten' fibres in biopsies taken from the trapezius muscle and suggested that hypoxia may have been the cause of this morphological finding. The change was not caused by a decrease in capillary density, because the number of capillaries was the same in FM patients and controls. The same investigators found decreased levels of adenosine triphosphate (ATP), adenosine diphosphate (ADP) and phosphoryl creatinine (PC), together with increased levels of adenosine monophosphate and creatine. They described discrete changes in muscle morphology and concluded that there were two possible explanations for these findings: (i) the chemical changes were secondary to hypoxia; (ii) there is a metabolic change that leads either to a defect in the synthesis of energy-rich phosphates or to increased degradation of these substances [9, 19]. Lund *et al.* [8] found evidence of pathological distribution of muscle surface oxygenation. The measurements of tissue oxygen pressure fields were performed with an MDO (Mehrdraht Dortmund Oberfläche) oxygen electrode. It was placed on the surfaces of the trapezius and the brachioradialis muscles. Abnormally low oxygen tension was found in all FM patients [8].

Our results are also in accordance with the findings of other investigators: in chronic trapezius myalgia, Larsson *et al.* [20] found a correlation between pain and reduced blood flow, supporting the hypothesis that local muscle pain is related to local temporary hypoxia. In a group of patients with FM, Vaeroy *et al.* [21] recorded low levels of blood flow in the skin. Reduced blood flow in FM has also been recorded by Bennett *et al.* [22] and Bäckman *et al.* [23].

Correlation of muscle blood flow with decreased levels of ATP, ADP and PC and an increase in creatinine has been shown in other diseases, including rheumatoid arthritis (RA). Oka *et al.* [24] recorded reduced muscle blood flow in RA patients. Nordemar *et al.* [25] found decreased levels of ATP, ADP and PC and increased creatinine levels in RA patients.

What is the reason for this reduced blood flow? Frödin *et al.* [26] examined nail-fold capillary morphology and blood flow in FM patients and found only slight morphological abnormalities. This suggests that capillary abnormalities are not a prominent feature in FM. The disturbed microcirculation in FM may be due to abnormal regulation of capillary blood flow rather than morphological changes in the capillaries [26]. Another reason could be vasoconstriction of unknown pathophysiology. The regulation of the microcirculation is controlled by local metabolic factors, by sympathetic nervous activity and by hormonal factors [27].

The importance of sympathetic nervous activity in patients with FM is illustrated by the findings of the following authors: Bäckman *et al.* [23] found a lower hand-grip strength in FM patients than in controls before and after sympathetic blockade. A lower muscle relaxation rate was found in FM patients. The relaxation rate increased in patients during the sympathetic blockade. The efficiency of stellate ganglion blockade was evaluated by measuring skin blood flow, skin temperature and skin conductance responses. Bengtsson and Bengtsson [28] concluded that the reduction of pain and tender points by sympathetic blockade may have been due to an improvement in microcirculation. Furthermore, they hypothesized that sympathetic activity contributes to the pathogenesis of FM [28]. Bennett *et al.* [22] found an increased density of $\alpha 2$ receptors in FM patients, which predisposes them to cold and emotion-induced vasospasm. In the same study they recorded decreased blood flow before the beginning of the test. Coffman and Cohen [29] reported that $\alpha 2$ receptors are predominant in the control of sympathetic vasoconstriction.

If the secretion of noradrenaline is stimulated maximally, the blood flow through the muscle can decrease to about 25% of the normal rate [28]. One reason for this could be increased sympathetic nervous activity. It has been shown that sympathetic nervous activity is increased during static muscle contraction [30].

Vaeroy *et al.* [21] observed that the vasoconstrictor response to the cold pressure test in FM patients was significantly lower than in controls. The possibility that the basal sympathetic tone may be increased in the FM patients could not be excluded.

A hypothesis based on a single pathogenic factor relating to FM can be formulated on the basis of these findings: physical and psychological afferences produce a motor and a sympathetic efference. The result of the motor efference is high muscle tension. The result of the sympathetic efference is sympathetic nervous overactivity. The increased sympathetic nervous activity induces an increase in muscle tension and local vasoconstriction in the arterioles and precapillary sphincters in the fibromyalgic muscle and skin. Local vasoconstriction results in increased erythrocyte concentration and speed. The flux of erythrocytes decreases [31]. As a consequence, there is imbalance between oxygen supply and demand, local hypoxia, a decrease in the concentration of high-energy phosphate, morphological changes, ischaemia and pain. A hypothetical scheme of pathogenic interactions among factors that may be involved is shown in Fig. 1.

The results of this study support the hypothesis that local pain in FM is related to temporary hypoxia [31]. A pathological microcirculation is probably present in the skin above tender point areas in FM. Other non-tender areas or control points need to be examined in further studies. The involvement of the sympathetic nervous system in the pathogenesis of pain in FM should be considered.

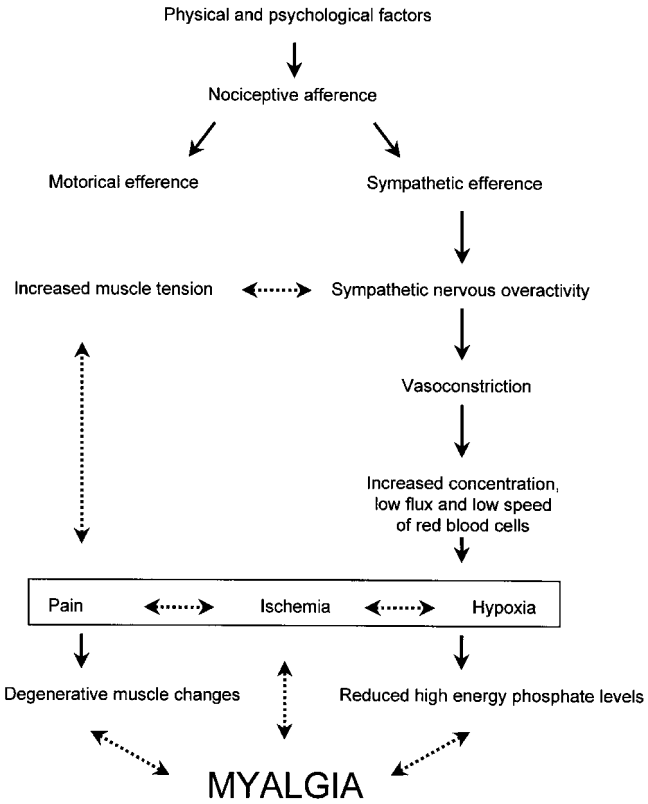


FIG. 1. Hypothetical pathogenic interactions of factors that may be involved in fibromyalgia.

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